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| ART UNIT | PAPER NUMBER |
|---|---|
| 1638 | |

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/723,083 | ALTOSAAR ET AL. | |
| | Examiner | Art Unit | |
| | Maria Teresa Samson | 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-49 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-49 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 26 November 2003 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 10/723,083.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-49 are pending.

### *Specification*

(A.) The disclosure is objected to because it contains embedded hyperlinks and/or other forms of browser-executable code. See page 17, line 3 and page 19, line 23. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01.

(B.) This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821 (a) (1) and (a) (2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Specifically, in figure 6, no sequence identifiers are given for GMCSF/ori.

Full compliance with the sequence rules is required in response to this office action. A complete response to this office action must include both compliance with the sequence rules and a response to the issues set forth herein. Failure to fully comply with both of these requirements in the time period set forth in this office action will be held to be non-responsive.

(C.) The drawings are objected to because the figure 4 cannot have a brief description on the legend of the figure.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(A.) Claims 1-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to a method of producing any GM-CSF from any source by transforming a cereal plant with a genetic construct comprising a regulatory region functional in a cereal plant that is operably linked to any GM-CSF coding sequence, a fragment, derivative of the GM-CSF coding sequence fused to a signal sequence or GM-CSF coding sequence that is optimized for expression in cereal plant or GM-CSF coding sequence encoding an N-terminal methionine residue or SEQ ID NO: 1 (whose coding sequence is optimized for expression in O. sativa, japonica) and to a transcriptional terminator, a transgenic cereal crop comprising said DNA molecule, a genetic construct comprising a regulatory region functional in a cereal plant operably linked to any GM-CSF coding sequence that is optimized for expression in cereal plants fused to a signal sequence or GM-CSF coding sequence encoding an N-terminal methionine residue and to a transcriptional terminator, a transgenic cereal plant or any plant comprising a DNA vector comprising SEQ ID NO: 1, a method of producing any GM-CSF coding sequence, a fragment or a derivative in any plant and said plant expresses GM-CSF and exhibits activity, a genetic construct comprising a regulatory region functional in a plant, operably linked with any GM-CSF coding sequence optimized for expression in a plant and a transcriptional terminator in a plant cell, seed comprising said DNA.

Applicant describe a genetic construct containing the Gt1 promoter as well as the glutelin signal sequence which is in-frame with the human GM-CSF mature coding sequence, a

transgenic rice comprising the genetic construct and said rice plants expresses human GM-CSF and support proliferation of TF-1 cells.

Applicant does not describe a genetic construct containing a regulatory region that is linked to SEQ ID NO: 1 or a nucleic acid molecule encoding any GM-CSF from any source or the coding sequence has been optimized, that is a fragment or a derivative of the coding sequence of GM-CSF and a transgenic plant comprising said genetic construct that produces GM-CSF.

Applicant does not describe the sufficient structural elements of GM-CSF that are required for function and that these structural elements are also present in nucleic acid molecules that encode any GM-CSF and particularly for any fragment or derivative thereof. The Applicant does not describe the sufficient structural elements of a representative number of nucleic acid molecules that encode GM-CSF and that have functional activity as evidence by the support of cell proliferation of TF-1 cells.

Claims 1-49 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1-49 are drawn to any GM-CSF coding sequence, or a fragment or a derivative of the GM-CSF coding sequence that is claimed solely by function and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and

Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, human GM-CSF mature coding sequence has been set forth, and shown to support proliferation of TF-1 cells. This DNA sequence is only described according to the functional characteristics of the protein; no structural relationship is described or used in the claims. Thus, one of skill in the art would be unable to predict the structure of other members of this genus by virtue of the instant disclosure. Therefore, the claims are not adequately described.

Hence, the specification fails to provide an adequate written description of the genus claimed.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the claimed nucleic acids, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

(B.) Claims 1-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a genetic construct containing the Gt1 promoter as well as the glutelin signal sequence which is in-frame with the human GM-CSF mature coding sequence, a

transgenic rice comprising the genetic construct and said rice plants express human GM-CSF and can support proliferation of TF-1 cells, does not reasonably provide enablement for a genetic construct containing a regulatory region that is linked to SEQ ID NO: 1 or a nucleic acid molecule encoding any GM-CSF from any source or the coding sequence has been optimized, or is a fragment or is a derivative of the coding sequence of GM-CSF and a transgenic plant comprising said genetic construct, expresses the protein and can support cell proliferation of TF-1 cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to SEQ ID NO: 1 and to a nucleic acid molecule that encodes any GM-CSF from any source or a fragment, derivative of the coding sequence of GM-CSF, and said nucleic acid molecule is capable of supporting proliferation of TF-1 cells, a method of producing any GM-CSF from any source by transforming a cereal plant with a genetic construct comprising a regulatory region functional in a cereal plant that is operably linked to any GM-CSF coding sequence, or a fragment, derivative of the coding sequence of GM-CSF fused to a signal sequence or GM-CSF coding sequence that is optimized for expression in cereal plant or GM-CSF coding sequence encoding an N-terminal methionine residue or SEQ ID NO: 1 (whose coding sequence is optimized for expression in O. sativa, japonica) and to a transcriptional terminator, a transgenic cereal crop comprising said DNA molecule, a genetic construct comprising a regulatory region functional in a cereal plant operably linked to any GM-CSF coding sequence that is optimized for expression in cereal plants fused to a signal sequence or GM-CSF coding sequence encoding an N-terminal methionine residue and to a transcriptional

terminator, a transgenic cereal plant or any plant comprising a DNA vector comprising SEQ ID NO: 1, a method of producing any GM-CSF coding sequence, a fragment or a derivative in any plant and said plant expresses GM-CSF and exhibits activity, a genetic construct comprising a regulatory region functional in a plant, operably linked with any GM-CSF coding sequence optimized for expression in a plant and a transcriptional terminator in a plant cell, seed comprising said DNA.

Applicant's teachings only provide guidance for a genetic construct containing the Gt1 promoter as well as the glutelin signal sequence which is in-frame with the human GM-CSF mature coding sequence, a transgenic rice comprising the genetic construct and said rice plants express human GM-CSF and support proliferation of TF-1 cells.

Applicant does not describe a genetic construct containing a regulatory region that is linked to SEQ ID NO: 1 or a nucleic acid molecule encoding any GM-CSF from any source or a coding sequence that has been optimized, or is a fragment, or is a derivative of the coding sequence of GM-CSF and a transgenic plant comprising said genetic construct, a transgenic plant comprising said DNA and said plant expresses the protein and can support cell proliferation of TF-1 cells.

The specification does not teach making DNA molecules that encode any GM-CSF from any source, which can be used to support proliferation of TF-1 cells. The specification does not exemplify transforming any plant with SEQ ID NO: 1 to support proliferation of TF-1 cells much less using any sequences that encode any GM-CSF from any source with the full scope of the claims and does not teach to make them.

In addition, the specification does not provide any guidance with regard to what structural features are required in a nucleic acid that can support proliferation of TF-1 cells, and the claims are drawn to a multitude of sequences.

The biological activity of GM-CSF is mediated by binding to specific receptors. Kaushansky et al generate a series of hybrid molecules containing various proportions of human- and murine-specific amino acid sequences and assayed for species-specific activity against human and murine marrow target cells (PNAS, 86: 1213-1217, abstract). Only the hybrid molecule that contains hGM-CSF-specific residues between positions 38 and 48 and between positions 95 and 111 stimulated proliferation of human marrow progenitor cells (page 1216, column 2, third paragraph). Furthermore, only hybrids containing hGM-CSF sequence from Glu-38 to Thr-111 could compete with the native molecule for binding to the cell surface receptor, suggesting that both the N-terminal and the C-terminal region identified by the functional analysis of hybrid proteins are critical for the binding of GM-CSF to its cell surface receptor (page 1216, column 2, fourth paragraph). Thus, transgenic plant comprising a genetic construct comprising a fragment or a derivative of the coding sequence of hGM-CSF may not contain this region that is required for binding to the receptor and thus for activity.

In addition, despite a high degree of sequence homology between human GM-CSF and murine GM-CSF, hGM-CSF fails to stimulate murine progenitor or mature blood cells and mGM-CSF fails to stimulate colony formation in cultures of human marrow progenitors (page 1213, abstract; column 1, second paragraph). Thus, GM-CSF from other source may not support proliferation of TF-1 cells.

Furthermore, the claims also encompass plants transformed with a genetic construct containing a regulatory region that is linked to a nucleic acid molecule encoding any GM-CSF from any source. Yet, transforming plants with a nucleic acid molecule encoding any GM-CSF from any source may not produce a functional protein since the protein may not be process by the plant properly. For example, when unmodified crystal protein genes are fused with expression signals used in the plant nucleus, protein production is quite poor compared to that of similar transcription units containing typical plant marker genes (Schnepf et al., Microbiology and Molecular Biology Reviews, 62:775-806, 1998; page 793, column1, second paragraph). However, truncation of the unmodified genes to synthesize only the toxic portion of the protein typically results in much improved, but still comparatively low, expression (Schnepf et al., Microbiology and Molecular Biology Reviews, 62:775-806, 1998; page 793, column1, second paragraph).

Further modification of the original Bt protein has also led to an increase in expression level of Bt in plants. For example, when the *Bacillus* sequences are extensively modified, with synonymous codons to reduce or eliminate the potentially deleterious sequences and generate a codon bias more like that of a plant, expression improves dramatically (Schnepf et al., Microbiology and Molecular Biology Reviews, 62:775-806, 1998; page 793, column1, second paragraph). The relatively A+T-rich *Bacillus* DNA contains a number of sequences that could provide signals deleterious to gene expression in plants, such as splice sites, poly(A) addition sites, ATTTA sequences, mRNA degradation signals, and transcription termination sites, as well as a codon usage biased away from that used in plants (Schnepf et al., Microbiology and Molecular Biology Reviews, 62:775-806, 1998; page 793, column1, second paragraph). Thus,

transforming the plant with a genetic construct containing a regulatory region that is linked to a nucleic acid molecule encoding any GM-CSF from any source may not be process properly in the plant, leading to an absence or low level of expression of the protein.

The applicant discloses SEQ ID NO: 1 whose coding sequence has been optimized for expression in O. sativa, japonica but does not exemplify transforming a plant with SEQ ID NO: 1 and said plant expresses a functional protein that can support the proliferation of TF-1 cells.

The applicant not only fails to teach the full scope of the claims but also fail to teach the possible side-effect of transforming plants with GM-CSF. GM-CSF is glycosylated. Plant glycosylation differs from mammalian systems. Glycosylation of foreign proteins in plants could be immunogenic to patients (Sardana et al., Transgenic Research, 11:521-531, 2002, page 529, column 2, first paragraph). Thus, further testing in humans is needed to verify if glycosylation could be immunogenic to patients.

Additionally, extensive further experimentation would be required to isolate and clone other nucleotide sequence that encodes any GM-CSF and to determine whether the sequences are capable of supporting proliferation of TF-1 cells.

Moreover, the specification does not teach how to use the method of producing any GM-CSF by transforming a cereal plant or any plant with a genetic construct comprising SEQ ID NO: 1 or a regulatory region that is operably linked to any GM-CSF (coding sequence, a fragment, derivative, coding sequence is optimized for expression or coding sequence encodes an N-terminal methionine residue) and to a transcriptional terminator, and said plant express a functional protein that can support proliferation of TF-1 cell.

Thus, given the limited teachings and guidance by Applicant, the nature of the art and the unpredictability of the art, undue trial and error experimentation would have been required by one of skill in the art at the time of Applicant's invention to use the nucleic acid of SEQ ID NO: 1 and to screen through a myriad of nucleotide sequence that encodes GM-CSF to find those that are hGM-CSF-like genes. Therefore, it would require undue experimentation for one skilled in the art to make/or use the claimed invention.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32, 34 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claim is included in all rejections.

(A.) Claims 32 and 34 are indefinite in their recitation of "a DNA vector comprising the genetic construct". A DNA vector is a genetic construct. Thus, it is unclear how this further limits the claim.

(B.) The term "between about 60% to 100%, preferably 80% to 100%, more preferably 95% to 100%" in claim 38 is a relative term which renders the claim indefinite. The term " between about 60% to 100%, preferably 80% to 100%, more preferably 95% to 100%" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(A.) Claims 36, 37 and 41 are rejected under 35 U.S.C. 102 (b) as being anticipated by Sardana et al (Transgenic Research, 11: 521-531, 2002). Sardana et al disclosed a method of producing human GM-CSF in tobacco seeds. The DNA fragment encoding mature human GM-CSF is under the control of either Gt1 or Gt3, rice glutelin promoters. The Gt3 construct contained the Gt3 promoter, glutelin signal sequence and the first 24 nucleotides, encoding the N-terminal eight residues of the mature glutelin, were subcloned in-frame with the mature GM-CSF coding sequence followed by the Nos-terminator sequence from the nopaline synthase gene (page 524, column 2, second paragraph). The Gt1 construct contained the Gt1 promoter, glutelin signal sequence in-frame with the coding sequence of mature GM-CSF followed by the Nos-terminator sequence from the nopaline synthase gene (page 524, column 2, second paragraph). Southern analysis showed the absence of any rearrangements in the GM-CSF constructs in these plants (page 525, column 1, second paragraph). Transgenic tobacco seed extracts expressed the recombinant human GM-CSF protein up to a level of 0.03% of the total soluble protein (page

521, abstract). The seeds of F1 generation plants retained the biological activity of human GM-CSF protein indicating that the human coding sequence was stably inherited.

***Claim Rejections - 35 USC § 102/103***

(A.) Claim 38 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Sardana et al (Transgenic Research, 11: 521-531, 2002). Claim 38 requires that GM-CSF expressed from a plant exhibits between about 60% to 100%, preferably 80% to 100%, more preferably 95% to 100% of the activity of human GM-CSF.

Sardana et al disclosed a method of producing human GM-CSF in tobacco seeds. The DNA fragment encoding mature human GM-CSF is under the control of either Gt1 or Gt3 rice glutelin promoter. The Gt3 construct contained the Gt3 promoter, glutelin signal sequence and the first 24 nucleotides, encoding the N-terminal eight residues of the mature glutelin, were subcloned in-frame with the mature GM-CSF coding sequence followed by the Nos-terminator sequence from the nopaline synthase gene (page 524, column 2, second paragraph). The Gt1 construct contained the Gt1 promoter, glutelin signal sequence in-frame with the coding sequence of mature GM-CSF followed by the Nos-terminator sequence from the nopaline synthase gene (page 524, column 2, second paragraph). Transgenic tobacco seed extracts expressed the recombinant human GM-CSF protein up to a level of 0.03% of the total soluble protein. Seed-derived extracts from the Gt1 and Gt3 plants when added individually to the medium supported proliferation of TF-1 cells as assessed at 48 h (page 528, column 1, first paragraph). The positive control, *E- coli* derived GM-CSF, also supported proliferation of TF-1 cells whereas the seed extract from the non-transformed tobacco plant and protein extraction buffer added to assay medium did not supported TF-1 cell proliferation (page 528, column 1, first paragraph).

Sardana et al disclosed a method of producing human GM-CSF in tobacco seeds. Seed extracts from the Gt1 and Gt3 plants when added individually to the medium supported proliferation of TF-1 cells as claimed in the instant application but does not compare the activity to human GM-CSF. The examiner is unable to determine whether the prior art disclosure exhibits between about 60% to 100%, preferably 80% to 100%, more preferably 95% to 100% of the activity of human GM-CSF. The USPTO cannot conclude that the subject matter of the claim would have been obvious since it cannot determine whether the activity is between about 60% to 100%, preferably 80% to 100%, more preferably 95% to 100% of the activity of human GM-CSF. The USPTO/examiner is not in a position to make either a conclusion of "inherency/anticipation" or "obviousness" since the record does not allow one to determine if and how the claimed subject matter differs from the prior art. Accordingly, the burden shifts to applicant to provide evidience that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 6-7, 11-13, 16, 17, 21-23, 26, 27 and 36-42 rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al (United Stated Patent No.: US 6,288,302, 11 September 2001) in view of Sardana et al (Transgenic Research, 11: 521-531, 2002).

Yu et al disclosed a method for mass production of a gene product in plants (column 1, line 21). Yu et al disclosed transforming Oryzae sativa L. cv. Tainung, a Japonica type of rice, with a construct comprising a GUS reporter gene driven by an α-amylase promoter and the GUS reporter gene is followed by a transcriptional terminator. Southern blot analysis showed that the foreign genes were integrated into the genomes of transgenic plants and histochemical localization of GUS activity in one transgenic plant (T1) revealed that the rice α-amylase promoter functions in all cell types of the mature leaves, stems, sheaths and roots but not in the very young leaves (column 14, line 45).

Yu et al do not disclosed a method of producing GM-CSF in a rice plant specifically a japonica cultivar.

The teachings of Sardana et al are discussed above.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing a polypeptide in a rice plant specifically a japonica cultivar with a construct comprising a GUS reporter gene driven by an α-amylase promoter and the GUS reporter gene is followed by a transcriptional terminator as taught by Yu et al to substitute a DNA molecule encoding GM-CSF as described in Sardana et al. One of ordinary skill in the art would have been motivated to do so because Yu et al recite according to this invention, a protein expression system is developed in which the foreign gene will be linked downstream of the α-amylase gene promoter and signal sequence and expressed throughout the

whole plant or in the germinating seed of transgenic rice (column 7, line 56). Yu et al further recite that it is thus intended to explore the potential of rice plant for producing commercially interesting proteins, e.g. the hepatitis B virus surface antigen S2 and the human interleukin-2 (column 7, line 66). Thus, the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art, at the time it was made, especially in the absence of evidence to the contrary.

(B.) Claims 7-9, 14, 15, 18, 19, 24, 25, 28, 29, 32, 34, 45, 46 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al, taken with Sardana et al, and further in view of applicant's admitted state of the prior art.

The teachings of Yu et al and Sardana et al are discussed above.

Yu et al and Sardana et al do not disclose a method of producing GM-CSF wherein the coding sequence is operably linked to a signal sequence or the coding sequence is optimized for expression in a rice plant specifically a japonica cultivar.

The specification teaches the use of a 72 basepair Gt1 signal sequence operably linked to the hGM-CSF (page 23, paragraph 72) and optimizing sequences for particular plants including rice (page 16, paragraph 57 and page 17, paragraph 57). These were known in the art at the time of filing. Thus, the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art, at the time it was made, especially in the absence of evidence to the contrary.

(C.) Claims 43, 44, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sardana et al taken with applicant's admitted state of the prior art.

The teachings of Sardana et al are discussed above.

Sardana et al do not disclose a transgenic plant comprising GM-CSF wherein the coding sequence is operably linked to a signal sequence or the coding sequence is optimized for expression in a rice plant specifically a japonica cultivar.

The specification teaches the use of a 72 basepair Gt1 signal sequence operably linked to the hGM-CSF (page 23, paragraph 72) and optimizing sequences for particular plants including rice (page 16, paragraph 57 and page 17, paragraph 57). These were known in the art at the time of filing. Thus, the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art, at the time it was made, especially in the absence of evidence to the contrary.

Claims 10, 20, 30, 31, 33 and 35 are free of prior art.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Teresa Samson whose telephone number is 571-272-3110. The examiner can normally be reached on 7:00-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's

Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Maria Teresa Samson, Ph.D
April 6, 2005

ELIZABETH MCELWAIN
PRIMARY EXAMINER